NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY

SUBMARINE BASE, GROTON, CONN.

REPORT NUMBER 956

CO_2 RETENTION AND ECG CHANGES IN EXERCISE DURING PROLONGED HYPERBARIC N_2-O_2 BREATHING

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Naval Medical Research and Development Command
Research Work Unit M0099-PN. 002-7060

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SUMMARY PAGE

THE PROBLEM

The vast majority of U. S. Navy diving is at relatively shallow depths (less than 200 feet of sea water gauge) and utilizes air or a nitrogen-oxygen mixture. The clinical significance of a marked CO_2 retention in exercise at increased ambient pressure on the functional integrity of the heart and circulation has not been evaluated in a systematic way.

FINDINGS

Our findings show a significant hypoventilation and hypercapnia during exercise with a load of 150 watts at 4.03 ATA (100 fswg). At 7.00 ATA (198 fswg) there was a slight but significant elevation of P_{ACO_2} at rest and a depression of the ventilatory response to exercise at both 50 and 125 watts associated with a marked CO_2 retention.

Arrhythmias during exercise were infrequent. However, arrhythmias were found at 4.03 and 7.00 ATA with workloads of 150 and 125 watts, respectively. At 4.03 ATA, premature atrial contractions (PAC) were noted at 150 watts in two subjects during four separate testing sessions. At 7.00 ATA, PAC's were observed at 125 watts in two subjects. One subject developed premature ventricular contractions (PVC's) during three different tests at 125 watts. Arrhythmias occurred only in those exercise tests which produced a marked CO_2 retention at increased pressure.

APPLICATION

Breathing N_2-O_2 mixtures at 4.3 ATA (100 fswg) delineates a threshold for limitation of moderate to heavy exercise. Beyond this level, heavy exercise levels will require a less dense inert gas, very low breathing resistance equipment, and/or a reduction in the rate of work (exertional level).

ADMINISTRATIVE INFORMATION

This investigation was conducted as part of Naval Medical Research and Development Command Research Work Unit M0099-PN.002-7060 -- "Regulation of respiration and circulation at rest and during exercise in dives to shallow and intramediate depths". The present report was submitted for review on 17 June 1981, approved for publication on 26 August 1981 and has been designated as NavSubMedRschLab Report No. 956.

PUBLISHED BY THE NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY

ABSTRACT

Respiratory function (V_E, V_{O_2}, V_{CO_2}, R and $P_{A_{CO_2}}$) was measured in ten subjects at rest and exercise during prolonged hyperbaric chamber exposure to 2.52, 2.82, 4.03, and 7.00 atmospheres absolute (ATA). At 4.03 ATA, the ventilatory response to exercise was found depressed at 150 watts. Increased $P_{A_{CO_2}}$ indicated CO_2 retention. At 7.00 ATA there was a slight but significant elevation of $P_{A_{CO_2}}$ at rest and a depression of the ventilatory response to exercise at both 50 and 125 watts associated with a marked CO_2 retention.

Arrhythmias were found at 4.03 and 7.00 ATA with workloads of 150 and 125 watts, respectively. At 4.03 ATA, premature atrial contractions (PAC) were noted at 150 watts in two subjects during four separate testing sessions. At 7.00 ATA, PAC's were observed at 125 watts in two subjects. One subject developed premature ventricular contractions (PVC's) during three different tests at 125 watts. Arrhythmias occurred only in those exercise tests which produced a marked CO_2 retention at increased pressure.

INTRODUCTION

Hypoventilation and CO_2 retention under pressure have been observed frequently at pressures of 4.00 atmospheres absolute (ATA) or 99 feet sea water gauge (fswg) and greater (5, 8, 13, 14, and 21). The limitation of ventilation under pressure has been attributed to the increased respiratory resistance to breathing denser gas mixtures. Both the increased ambient inert gas pressure and the increased oxygen tension have been found to play a role in hypoventilation (8, 14). The clinical significance of a marked CO_2 retention in exercise at increased pressure on the functional integrity of heart and circulation has not been evaluated in a systematic way. During a series of saturation-excursion dives utilizing N_2-O_2 mixtures at pressures ranging between 2.52-7.00 ATA (50-198 fswg), we measured respiratory function at rest and exercise (two work loads) and simultaneously monitored the electrocardiogram (lead II, occasionally I or III).

MATERIALS AND METHODS

Four dives were carried out in the hyperbaric chamber complex at the Naval Submarine Medical Research Laboratory in Groton, Connecticut. The pressure profiles of the dives are shown in Figure 1. In SHAD I, two subjects were exposed to 2.52 ATA (50 fswg) for a period of 29 days. During SHAD II two subjects lived at a depth of 2.82 ATA (60 fswg) for 27 days with excursions upward to 1.15 ATA (5 fswg) and downward to 8.58 ATA (250 fswg). The mean oxygen tension equaled 0.57 ATA. SHAD III was an 8-day compressed air dive to 2.52 ATA (50 fswg) with six daily 8-hour excursions to 4.03 ATA (100 fswg). This hyperoxic dive had an average O_2 tension of 0.63 ATA. Measurements of respiratory function in rest and exercise were performed at the same time each day at excursion depths of 4.03 ATA (100 fswg). Three subjects participated in this dive. In NISAT I, three subjects lived and worked at a depth of 7.00 ATA (198 fswg) for 7 days, followed by a 7-day decompression period. No excursion dives were performed in NISAT I. The oxygen tension was initially at 0.21 ATA oxygen, and raised to 0.30 ATA after 9 hours.

The ventilatory response of 10 divers was measured at rest and at two work loads. During SHAD I, II, and III, 100 and 150 watts were utilized. During NISAT I the work load was reduced to 50 and 125 watts, because of the expected marked increase in resistance to breathing at this higher pressure.

An open circuit system was used to measure minute ventilation tidal volume, O_2 uptake, CO_2 excretion, and respiratory exchange ratio. Heart rate was also determined from the ECG recording. The subjects were breathing through a high velocity Otis-McKerrow valve (Warren E. Collins No. 22331). Mixed expired air was collected in Douglas bags (100 liter bags at rest and 200 liter bags at exercise) during the last 2 minutes of a 5-minute period at rest and the two 10-minute exercise loads. Tubing connecting the respiratory valve with the Douglas bags had a 1½-inch internal diameter. End tidal gas was monitored continuously breath by breath with a respiratory mass spectrometer (Scientific Research Instruments Corps., MS-8 (Med Spec I). Vinyl tubing collecting the samples for the mass spectrometer was placed in the center of the respiratory valve through a rubber stopper. The sampling flow rate was 60 cc/min. The volume of exhaled gas was measured inside the chamber with a Parkinson-Cowan dry gas meter (Model 9001E).

The subjects exercised on a Warren E. Collins Pedal-Mode ergometer, which uses an induction brake. The work load remains constant at any pedal rate above 35 rpm. The subjects were instructed to pedal at 60 rpm because of biomechanical considerations. Each subject wore a noseclip throughout the procedures.

Data on respiratory functions during exercise obtained in the first experiment (SHAD I) were not utilized because the subjects were found to have become deconditioned during the 30-day exposure period. The exercise tests were only performed four times during the whole 30-day period which did not prove sufficient to prevent deconditioning as indicated in the increasing pulse rate during the exercise tests in the later part of the hyperbaric exposure. As a result of this experience, subjects in subsequent dives were required to exercise more frequently during the hyperbaric exposures, in addition to the exercise tests in which measurements were made.

Standard six lead electrocardiograms (I, II, III, AVR, AVL, AVF) were taken before and after each tests. Lead I, II, or III (generally II) was monitored during the test. Each of the tracings were examined for changes in P waves, P-R interval, QRS intervals, S-T segment, and T waves. Any aberrant conduction patterns were noted. In NISAT I the partial pressure of oxygen was initially maintained at 0.21 ATA with the nitrogen partial pressure at 6.79 ATA (191 fswg). Between 1-2 hours after pressurization to 7.00 ATA (198 fswg), two of the divers experienced severe lethargy, slurred speech, difficulty in breathing and vomiting. The oxygen partial pressure was then raised to 0.30 ATA and the symptoms disappeared rather quickly thereafter. This episode will be analyzed in more detail in the discussion section.

RESULTS

Figure 1 shows the profiles of the four dives. Data obtained during SHAD II on minute volume, resting respiratory rate, and tidal volume during the 27-day period of hyperbaric exposure showed no significant changes except a trend toward an increase in tidal volume during the hyperbaric exposure. The frequent excursion dives did not have an effect on basic respiratory functions.

The exercise tests performed during SHAD II at 100 and 150 watts did not show any significant changes in minute volume, tidal volume, and alveolar P_{CO_2} tension, except for a decrease in respiratory rate at the 150-watt load and in heart rate at 100 watts when compared to predive controls (Table 1). Daily 8-hour excursion dives to depth equivalent to 4.03 ATA (100 fswg) from a saturation depth of 2.52 ATA (50 fswg) during SHAD III had no significant effects on minute volume and respiratory rate measured under resting conditions lying in the supine position. However, the tidal volume, CO_2 excretion, and O_2 consumption increased during hyperbaric exposure compared to predive controls. The alveolar CO_2 tensions were not affected (Table 2). Exercise tolerance tests at 100 watts showed an increase in tidal volume which was nearly compensated by a decrease in respiratory rate and resulted only in a minor rise in minute volume. However, at 150 watts,

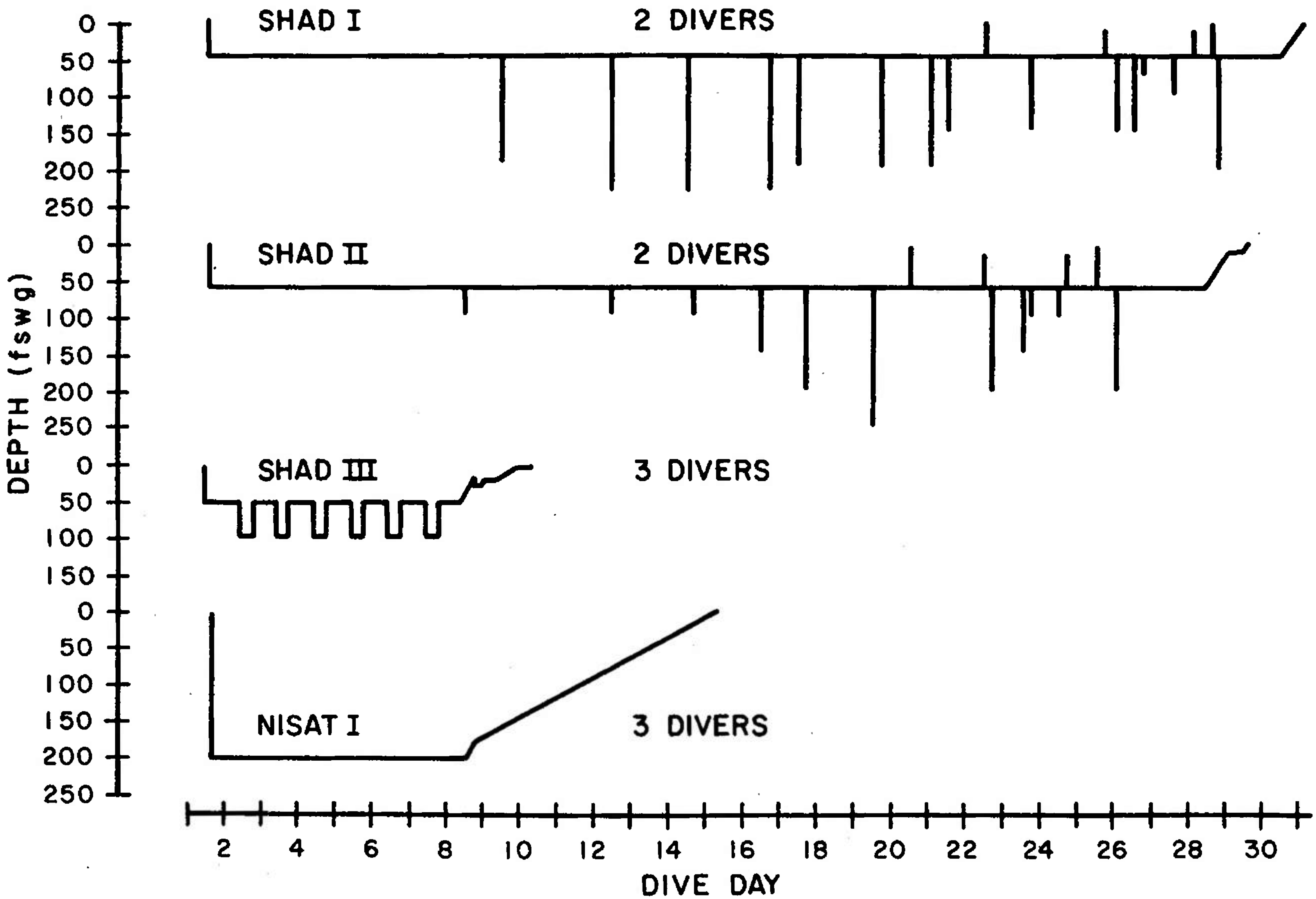

Figure 1. Dive Profiles

TABLE 1

EFFECT OF 27 DAYS OF EXPOSURE TO 2.82 ATA (60 FSWG) ON RESPIRATORY FUNCTION (MINUTE VOLUME, TIDAL VOLUME, RESPIRATORY RATE, AND ALVEOLAR CO_2 TENSION) AND HEART RATE DURING REST (SITTING ON BICYCLE) AND AT WORKLOADS OF 100 AND 150 WATTS (SHAD II)

		MINUTE VOLUME ℓ/min., BTPS			TIDAL VOLUME ℓ/min., BTPS			RESPIRATORY RATE breaths/minute			P_{ACO_2} mm Hg			HEART RATE beats/minute		
		Pre-Dive	Dive	Post-Dive	Pre-Dive	Dive	Post-Dive	Pre-Dive	Dive	Post-Dive	Pre-Dive	Dive	Post-Dive	Pre-Dive	Dive	Post-Dive
REST	Mean	14.73	15.78	11.49	0.84	1.04	0.75	18.0	15.2	15.3	34.5	35.5	33.6	79.8	81.3	89.5
	SEM	2.50	1.56	2.14	.16	.10	.09	2.1	0.9	1.8	1.2	1.5	1.6	10.2	3.4	2.9
	N	4	8	4	4	8	4	4	8	4	3	8	4	4	7	4
100 WATTS	Mean	44.00	42.10	44.76	2.05	2.13	1.85	21.3	20.2	24.3	35.7	37.5	34.9	135.3	126.3†	156.3*
	SEM	1.85	2.08	4.15	.04	.12	.21	1.2	1.4	1.8	1.1	1.4	1.8	5.2	8.1	5.7
	N	3	8	4	3	8	4	3	8	4	3	8	4	3	7	4
150 WATTS	Mean	67.50	60.40	65.80	2.36	2.39	2.33	28.7	25.4†	28.2	36.2	39.8	33.5	173.7	164.3	177.3
	SEM	4.39	2.81	2.60	.07	.13	.08	2.0	3.0	0.5	1.4	2.5	1.9	2.7	3.9	4.3
	N	3	8	4	3	8	4	3	8	4	3	8	4	3	7	4

*Statistically different from control at 5% confidence level
†Statistically different from recovery at 2% confidence level

TABLE 2

EFFECT OF DAILY 8-HOUR EXCURSION DIVES TO DEPTHS EQUIVALENT TO 4.03 ATA (100 FSWG) FROM SATURATION DEPTH OF 2.52 ATA (50 FSWG) ON MINUTE VOLUME, TIDAL VOLUME, RESPIRATORY RATE, AVLEOLAR CO_2 TENSION AND RESPIRATORY GAS EXCHANGE DURING REST IN SUPINE POSITION (SHAD III)

			PREDIVE CONTROL	DIVE	POSTDIVE RECOVERY
1.	Minute Volume ℓ/min, BTPS	Mean	9.21	10.74	10.38
		SEM	.67	.41	1.21
		N	9	20	6
2.	Tidal volume ℓ/min, BTPS	Mean	0.73	0.93*	0.80
		SEM	.07	.05	.10
		N	9	20	6
3.	Respiratory Rate/ minute	Mean	13.8	12.1	13.4
		SEM	1.1	.6	.8
		N	9	20	6
4.	P_ACO_2, mm Hg	Mean	36.6	36.2	37.5
		SEM	1.1	0.7	1.0
		N	10	20	6
5.	$\dot{V}_{CO_2}$ ml/minute, STPD	Mean	263	329 *	321
		SEM	17	15	32
		N	9	20	6
6.	$\dot{V}_{O_2}$ ml/minute, STPD	Mean	281	366 *	348
		SEM	17	14	22
		N	9	20	6
7.	R	Mean	0.95	0.90	0.91
		SEM	.02	.03	.04
		N	9	20	6

* Statistically significantly different from controls at the 5% confidence level and better

the ventilatory response was depressed during exposure to 4.03 ATA (100 fswg)(SHAD III), resulting in a significant CO_2 retention as indicated in the rise of the alveolar CO_2 tension (Table 3). Both CO_2 excretion and O_2 consumption at 100- and 150-watt work loads showed a trend towards an increase during exposure to 4.03 ATA (100 fswg)(SHAD III) as seen in Table 4. During exposure to 7.00 ATA (198 fswg), the alveolar CO_2 tension is increased even during resting conditions in the supine position (Table 5). The exercise tolerance tests with reduced work loads of 50 and 125 watts show a marked CO_2 retention, as indicated in the rise of the alveolar CO_2 tension in both work loads and even during the sitting position prior to the beginning of exercise. The ventilatory depression ($\dot{V}_E$) is significant at the 125-watt level, although trends in this direction are shown also in the sitting position and at the 50-watt work load (Table 6). Increase in CO_2 excretion occur during both exercise work loads (Table 7). Data on end tidal CO_2 tension obtained in SHAD II, SHAD III, and NISAT I were plotted against oxygen consumption ($\dot{V}O_2$) in Figure 2. Elevating the ambient pressure from 1.00 to 4.03 ATA causes only a slight rise in $P_{A_{CO_2}}$ while a further increase in pressure to 7.00 ATA produces a spectacular elevation of end tidal P_{CO_2}.

In Figure 3, the factors determining respiratory and circulatory responses to work loads under pressure (respiratory minute volume (V_E), tidal volume (V_T), respiratory frequency, and heart rate) are plotted against $\dot{V}O_2$. It is readily apparent that the decrease in respiratory frequency is responsible for the decrease in V_E at higher pressures. The bradycardia effect of increased ambient pressure adds another important constraining factor to the oxygen transport.

The exercise tracings from all four dives demonstrated increases in the height of the P and T waves, and shortening of the Q-T intervals compared to predive exercise controls. During near maximal stress, most of the subjects' tracings demonstrated minor changes in the S-T segments characterized by a slight depression (less than 1 mm) of the segment and a rapid rise from the J-point to the T-wave.

Arrhythmias during exercise were infrequent. None were observed in SHAD I or SHAD II: in SHAD III, while at excursion depth (4.03 ATA, 100 fswg), occasional premature atrial contractions (PAC's) were noted at work loads of 150 watts in two of the subjects during four separate testing sessions. In NISAT I, occasional PAC's were observed at a work load of 125 watts in two subjects (B and T). One subject (T) developed premature ventricular contractions (PVC's) during three different tests whenever work load was increased to 125 watts. On dive day 5, at 125 watts, rare PVC's were noted; on dive day 6 he failed to complete the test due to physical exhaustion and, although no extrasystoles were noted during the tests, his tracings demonstrated PVC's a few minutes after cessation of exercise (Figure 4). On dive day 7, the exercise tolerance test was stopped after a few minutes at 125 watts by the physician present because of signs of exhaustion in the subject (cold sweat) and the appearance of PVC's; these extrasystoles continued during the immediate post-exercise recovery period (Figure 5).

TABLE 3

EFFECT OF DAILY 8-HOUR AIR EXCURSION DIVES TO DEPTHS EQUIVALENT TO 4.03 ATA (100 FSWG) FROM SATURATION DEPTH OF 2.52 ATA (50 FSWG) ON MINUTE VOLUME, TIDAL VOLUME, RESPIRATORY RATE, AND ALVEOLAR CO_2 TENSION DURING REST AND EXERCISE (SHAD III)

		PREDIVE CONTROL	DIVE	POSTDIVE RECOVERY
1. MINUTE VOLUME, ℓ/min, BTPS				
REST(Sitting on bicycle)	Mean	17.3	16.8	17.8
	SEM	1.7	1.0	1.4
	N	10	9	5
100 WATTS	Mean	47.5	53.1	54.3
	SEM	1.7	3.5	5.1
	N	9	9	5
150 WATTS	Mean	78.6	64.3*	79.2
	SEM	5.4	2.4	5.7
	N	9	9	5
2. TIDAL VOLUME, ℓ/min, BTPS				
REST(Sitting on bicycle)	Mean	1.07	1.16	1.05
	SEM	.08	.05	.08
	N	10	9	5
100 WATTS	Mean	1.77	2.22*	2.02
	SEM	.10	.11	.05
	N	9	8	5
150 WATTS	Mean	2.25	2.65*	2.46
	SEM	.11	.10	.12
	N	9	9	5
3. RESPIRATORY RATE, breaths/min.				
REST(Sitting on bicycle)	Mean	16.0	14.0	17.0
	SEM	.6	.9	.6
	N	10	9	5
100 WATTS	Mean	27.0	22.0*	27.0
	SEM	1.6	1.1	2.5
	N	9	9	5
150 WATTS	Mean	36.0	25.0*	33.0
	SEM	1.8	1.5	2.7
	N	9	9	5
4. ALVEOLAR CO_2, mm Hg				
REST(Sitting on bicycle)	Mean	31.7	32.9	33.2
	SEM	1.2	2.0	1.7
	N	11	9	5
100 WATTS	Mean	36.8	39.4	33.4*
	SEM	.6	2.1	.7
	N	10	9	5
150 WATTS	Mean	33.7	40.2*	31.1*
	SEM	.6	2.2	.5
	N	9	9	5

*Statistically significantly different from control at the 5% confidence level and better

TABLE 4

EFFECT OF DAILY 8-HOUR AIR EXCURSION DIVES TO DEPTHS EQUIVALENT TO 4.03 ATA (100 FSWG) FROM SATURATION DEPTH OF 2.52 ATA (50 FSWG) ON $\dot{V}CO_2$, $\dot{V}O_2$, AND R DURING EXERCISE (SHAD III)

		PREDIVE CONTROL	DIVE	POSTDIVE CONTROL
1. CARBON DIOXIDE EXCRETION ($\dot{V}CO_2$) ml/min STPD				
REST (Sitting on bicycle)	Mean	352	395	338
	SEM	30	46	43
	N	10	9	5
100 WATTS	Mean	1,402	1,781	1,515
	SEM	73	235	85
	N	9	9	5
150 WATTS	Mean	2,244	2,396	2,091
	SEM	188	221	131
	N	9	9	5
2. OXYGEN CONSUMPTION ($\dot{V}O_2$) ml/min STPD				
REST (Sitting on bicycle)	Mean	332	423	449*
	SEM	16	15	20
	N	10	9	5
100 WATTS	Mean	1,437	1,871	1,612
	SEM	57	231	56
	N	9	9	5
150 WATTS	Mean	2,152	2,378	2,177
	SEM	83	223	81
	N	9	9	5
3. RESPIRATORY EXCHANGE RATIO (R)				
REST(Sitting on bicycle)	Mean	1.06	1.03	0.87
	SEM	.08	.09	.06
	N	10	9	5
100 WATTS	Mean	0.98	0.97	0.93
	SEM	.03	.07	.03
	N	9	9	5
150 WATTS	Mean	1.03	1.03	0.96
	SEM	.05	.06	.04
	N	9	9	5

*Statistically significantly different from control at the 5% confidence level.

TABLE 5

EFFECT OF SATURATION DIVE TO 7.00 ATA (198 FSWG) BREATHING N_2-O_2 MIXTURES ON RESPIRATORY FUNCTION AND RESPIRATORY GAS EXCHANGE WHILE RESTING IN THE SUPINE POSITION (NISAT I)

		CONTROL	198 FEET	DECOMPRESSION	RECOVERY
MINUTE VOLUME ℓ/min, BTPS	Mean	11.0	10.6	11.2	14.2
	SEM	1.2	.5	.7	.9
	N	10	18	15	6
TIDAL VOLUME ℓ/min, BTPS	Mean	1.09	0.94	1.27	1.38
	SEM	.16	.07	.10	.16
	N	10	18	15	6
RESPIRATORY RATE/minute	Mean	10.9	11.3	8.8	10.3
	SEM	.7	.6	.4	.3
	N	10	18	15	6
P_{ACO_2} mm Hg	Mean	37.3	40.0 *	42.0 *	36.8
	SEM	1.3	1.9	1.2	2.2
	N	10	18	15	6
$\dot{V}_{CO_2}$ ml/minute, STPD	Mean	324	322	389 *	380
	SEM	17	28	22	22
	N	10	18	15	6
$\dot{V}_{O_2}$ ml/minute, STPD	Mean	335	346	379	414
	SEM	26	23	20	43
	N	10	18	15	6
R	Mean	0.96	0.93	1.02	0.92
	SEM	.04	.08	.06	.06
	N	10	18	15	6

*Statistically significantly different from controls at the 5% confidence level.

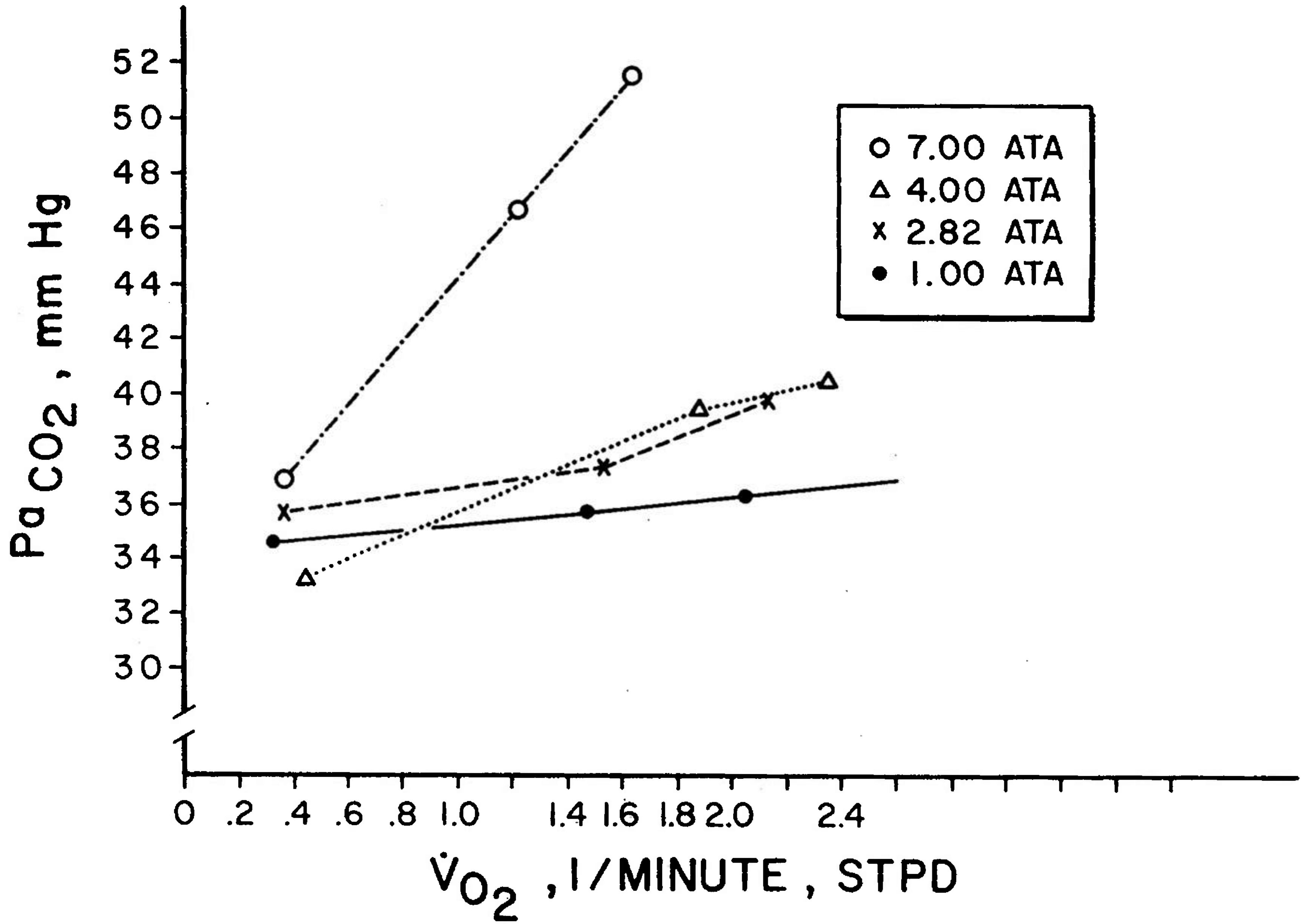

Figure 2. Relationship between end tidal CO_2 tensions (P_{ACO_2}) measured during SHAD II, SHAD III, and NISAT I to oxygen consumption ($\dot{V}_{O_2}$ ℓ/min, STPD). Data listed under 1.00 ATA represent the predive control data collected in SHAD II.

TABLE 6

EFFECT OF A SATURATION DIVE TO 7.0 ATA (198 FSWG) BREATHING N_2-O_2 MIXTURES ON RESPIRATORY FUNCTION (MINUTE VOLUME, TIDAL VOLUME, RESPIRATORY RATE, AND ALVEOLAR CO_2 TENSION) UNDER RESTING CONDITIONS (SITTING ON A BICYCLE) AND AT EXERCISE LOADS OF 50 AND 125 WATTS (NISAT I)

		SITTING(ON BICYCLE)				50 WATTS				125 WATTS			
		MINUTE VOLUME ℓ/min BTPS	TIDAL VOLUME ℓ/min BTPS	RATE/ MINUTE	$P_{A_{CO_2}}$ mm Hg	MINUTE VOLUME ℓ/min BTPS	TIDAL VOLUME ℓ/min BTPS	RATE/ MINUTE	$P_{A_{CO_2}}$ mm Hg	MINUTE VOLUME ℓ/min BTPS	TIDAL VOLUME ℓ/min BTPS	RATE/ MINUTE	$P_{A_{CO_2}}$ mm Hg
PREDIVE CONTROL	Mean	17.64	1.22	13.0	31.8	31.80	1.68	17.6	40.4	53.60	1.77	20.9	41.5
	SEM	2.70	.13	1.2	1.8	1.90	.17	2.0	.9	3.30	.13	1.9	1.1
	N	6	6	6	6	6	6	6	5	6	6	6	5
DIVE	Mean	16.90	1.44	11.9	36.9*	27.80	2.26*	14.7	46.6*	46.90*	2.32*	17.0	51.6*
	SEM	1.40	.16	1.0	1.0	1.30	.20	1.3	1.9	4.70	.15	1.7	2.9
	N	9	9	9	9	9	9	9	9	9	7	7	9
POSTDIVE RECOVERY	Mean	17.67	1.33	13.2	31.3	33.10	2.01	17.0	40.6	47.60	2.39*	20.1	40.5
	SEM	3.80	.16	.9	1.8	4.40	.30	1.7	.9	3.50	.18	1.8	1.0
	N	5	5	5	5	5	5	7	5	4	4	4	5

*Statistically significantly different from control at the 5% confidence level.

TABLE 7

EFFECT OF A SATURATION DIVE TO 7.0 ATA (198 FSWG) BREATHING N_2-O_2 MIXTURES ON RESPIRATORY GAS EXCHANGE ($\dot{V}CO_2$, $\dot{V}O_2$, R) AND HEART RATE UNDER RESTING CONDITIONS (SITTING ON A BICYCLE) AND AT EXERCISE LOADS OF 50 AND 125 WATTS (NISAT I)

		SITTING(ON BICYCLE)				50 WATTS				125 WATTS			
		$\dot{V}CO_2$ ml/min STPD	$\dot{V}O_2$ ml/min STPD	R	Heart Rate/ minute	$\dot{V}CO_2$ ml/min STPD	$\dot{V}O_2$ ml/min STPD	R	Heart Rate/ minute	$\dot{V}CO_2$ ml/min STPD	$\dot{V}O_2$ ml/min STPD	R	Heart Rate/ minute
PREDIVE CONTROL	Mean	389	395	0.96	81.0	1,104	1,117	1.03	116.2	1,290	1,364	0.94	142.0
	SEM	52	43	.03	4.0	91	94	.02	2.5	110	116	.01	2.8
	N	6	6	6	6	6	6	6	6	6	6	6	6
DIVE	Mean	465	349	1.22	75.0	1,346*	1,205	1.12	110.0	1,878 *	1,631	1.18	* 136.0*
	SEM	46	28	.08	1.9	166	126	.05	4.3	142	133	.06	4.0
	N	9	9	8	9	9	9	9	9	7	7	9	7
POSTDIVE RECOVERY	Mean	376	440	0.96	86.2	1,169	1,121	1.03	115.0	1,704	1,635	1.03	138.0
	SEM	73	128	.01	.7	167	123	.05	1.9	163	93	.06	4.5
	N	5	5	5	5	5	5	5	5	4	4	4	4

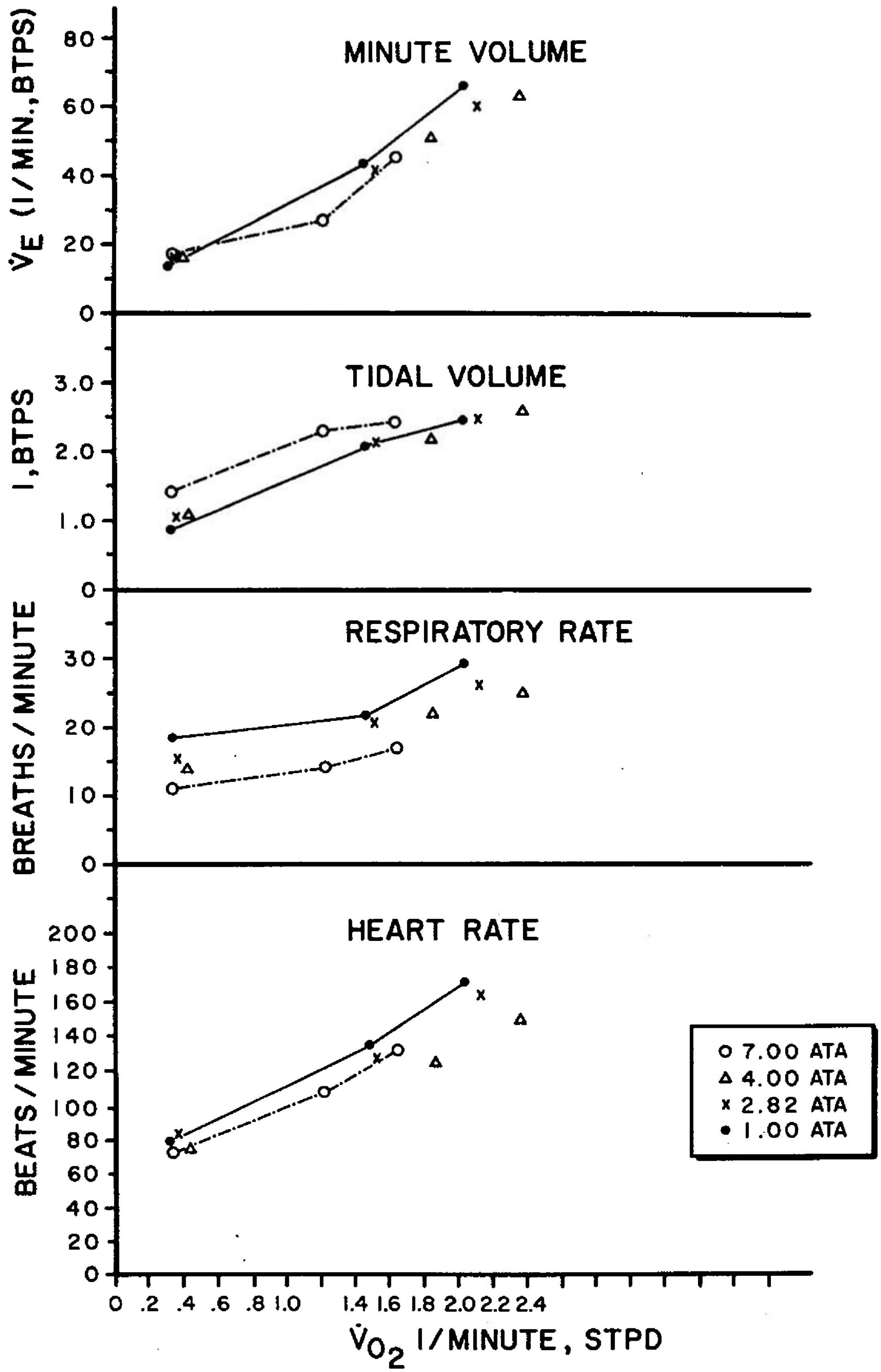

Figure 3. Relationship of ventilation, tidal volume, respiratory frequency, and heart rate to oxygen uptake. Measurements taken with subjects at rest and during exercise of 100 and 150 watts (SHAD II and SHAD III), and 50 and 125 watts (NISAT I).

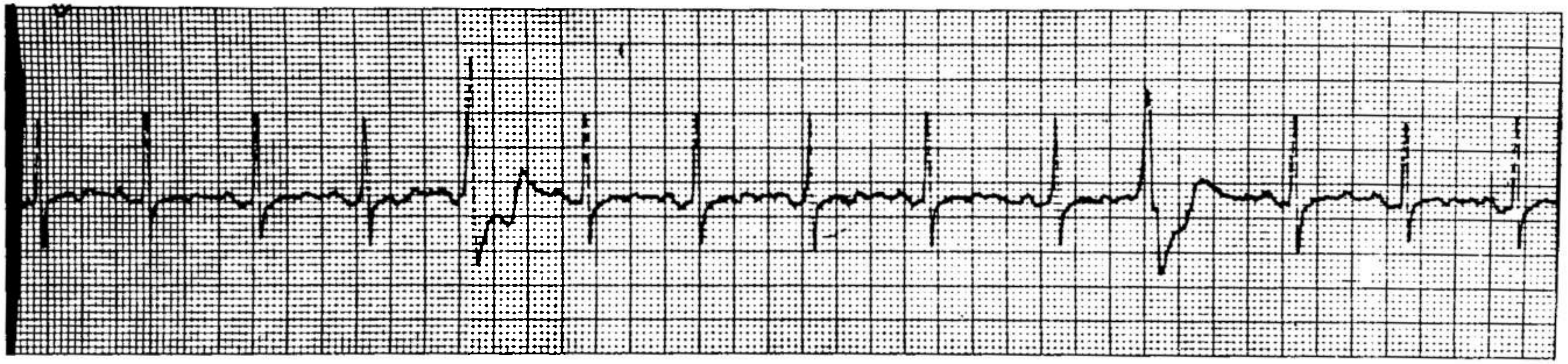

Figure 4. Tracings of diver T approximately 8 minutes after he became exhausted at work level of 125 watts. Note the premature ventricular contractions (NISAT I).

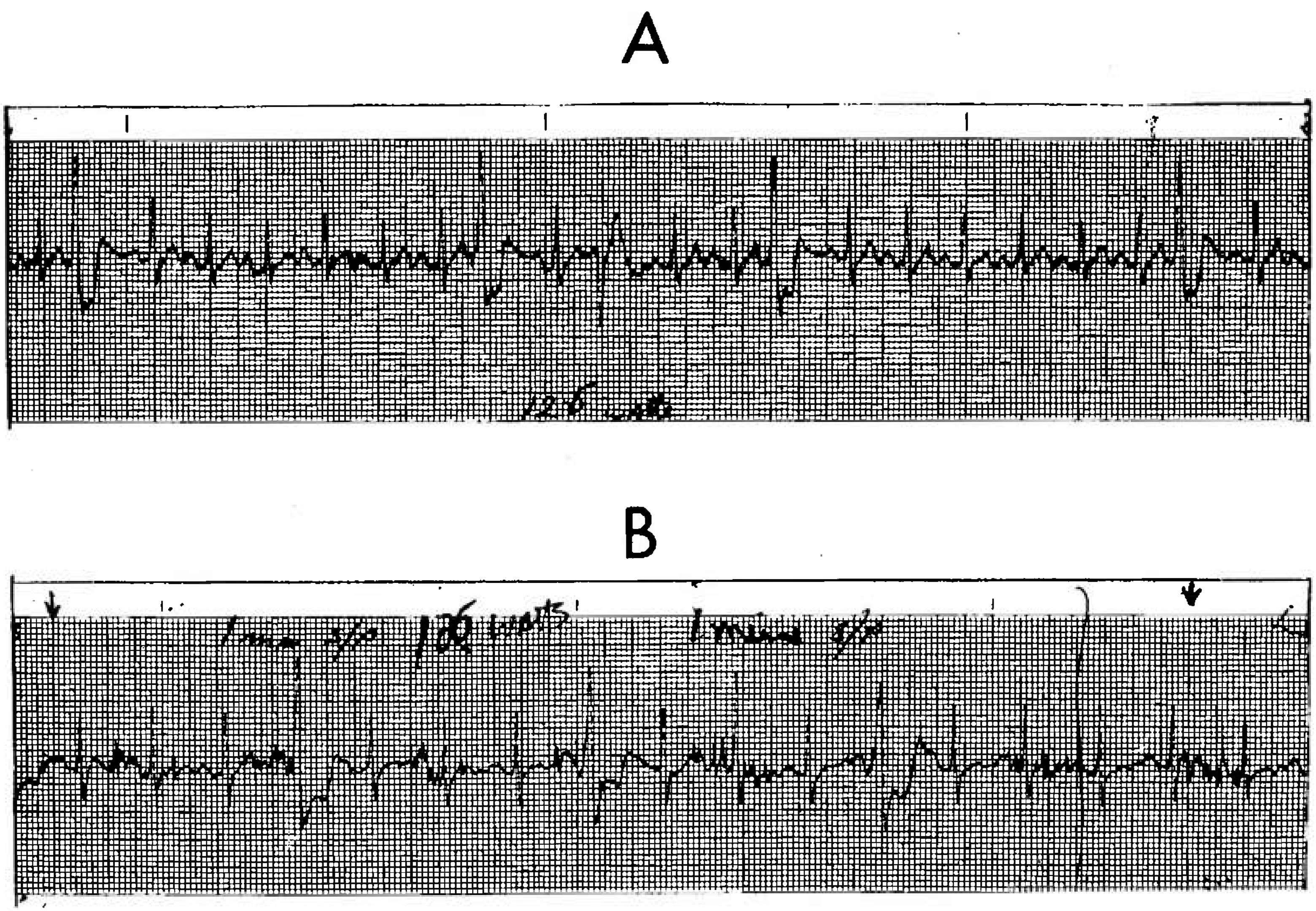

Figure 5. NISAT I. A. Tracing after approximately 6 minutes at a work load of 125 watts.
B. Tracing approximately 1 minute after termination of test.

DISCUSSION

SHAD I, II, and III

Our findings showing a significant hypoventilation and hypercapnia during exercise with a load of 150 watts at 4.03 ATA (100 fswg) are in agreement with the results obtained by Morrison, et al (21) during acute exposure to 4.00 ATA (99 fswg) and Lambertsen, et al (13) during a 14-day exposure with comparable exercise loads.

In the latter study the subjects were tested at a work load of 70% maximum capacity for a period of 6 minutes and the ventilatory measurements were made during the last 1.5 minutes of the exercise. During predive the average minute ventilation (6 subjects) was found to be 95.34 ℓ/min, and it fell 18% during chronic exposure to 4.03 ATA (100 fswg). In our experiment, 3 subjects carried out exercise at a work load of 150 watts for 10 minutes. Measurements were made during the last 2 minutes which showed an average minute ventilation of 78.5 ℓ/min under control conditions and a 19% fall during exposure to 4.03 ATA (100 fswg). The change in minute ventilation during exposure to 4.03 ATA (100 fswg) were produced by a decrease in respiratory frequency rather than a change in tidal volume (Figure 3). This is also in line with the observations by Lambertsen, et al (13) and Morrison, et al (21).

It is generally agreed that increased density of the inspired N_2-O_2 mixture causes an increase in respiratory resistance to breathing which in turn results in a limitation of the ventilatory response to exercise and leads to CO_2 retention (5, 8, 13, 14, and 21). Moreover, the CO_2 response curve was found to be reduced at increase pressure (7, 13) which may contribute to the reduced ventilatory response observed during exercise. It is difficult to assess the role of the bradycardia effect in the limitation of the exercise response under increased pressure. It has also been observed in other experiments under various pressures and different gas mixtures (8, 25, and 27). Breathing N_2-O_2 mixtures at 4.03 ATA (100 fswg) delineates a threshold for limitation of moderate to heavy exercise.

NISAT I

Exposure to 7.00 ATA (198 fswg) was indeed a stressful dive as suggested by the following three criteria. First, sensory functions and reaction time for all subjects were dramatically reduced at depth (20). Second, the divers felt distressed in numerous ways, including nausea, respiratory difficulty, thermal discomfort, narcosis, arthralgia and fatigue. Third, there were documented medical and physiological changes such as vomiting, EKG, and ECG changes, and slurred speech.

Impairing effects of normoxic (0.21 ATA) oxygen partial pressure to 7.00 ATA(198 fswg)

The possible cause of the initial signs and symptoms which occurred in NISAT I needs to be discussed in more detail. Between 1 and 2 hours after pressurization to 7.00 ATA (198 fswg), two of the divers experienced the onset of nausea and shortly afterwards developed vomiting. All three divers also showed symptoms of vertigo, slurred speech, and cold sensations not usually associated with nitrogen narcosis. Partial relief of the symptoms occurred during elevation of the P_{IO_2} from 0.21 ATA to 0.30 ATA. This was carried out over a 54-minute period beginning approximately 9 hours after reaching the saturation pressure of 7.00 ATA (198 fswg). The divers continued to experience nausea, to a lesser extent, until the morning of the third day when all divers were free of the described symptoms aside from feeling "slightly drunk". During dive day 2, all subjects reported the sensation of "heavy breathing" without orthopnea or ankle edema. The complaints of heavy breathing continued throughout the dive until well into the decompression phase. The exercise tests were begun on dive day 5. All subjects reported vague symptoms of "low energy levels," shortness of breath on minor exertion, and feeling tired after the tests. Diver E had to abort the bicycle ergometer test at 125 watts because of undue breathlessness on dive day 5.

During the initial period, one of the divers had electrocardiographic changes consisting of a lengthening of the P-R interval (from 0.14 seconds predive to 0.21 seconds). The P waves became progressively more flattened and disappeared, resulting in a nodal rhythm. Minor S-T elevations, rSR' complexes in the right precordial leads and diphasic T waves appeared during this period, indicating a right ventricular conduction delay. After 8 hours of breathing the increased oxygen concentration, the rSR' complexes and T wave changes had disappeared, and the P waves were more demonstrable. In the second diver PVC's had occurred during the initial period of 0.21 ATA oxygen, which disappeared after more oxygen was added (0.30 ATA). Such tissue hypoxia might result from interference of the oxygenation of human arterial blood. To examine this possibility, Saltzman, et al (24) studied pulmonary function in 3 divers breathing normoxic nitrogen at 7.00 ATA (198 fswg). The authors concluded that breathing normoxic nitrogen in a dry chamber did not adversely affect the P_{AO_2}, although a simultaneously elevated P_{ACO_2} suggested alveolar hypoventilation. The distressing symptom complex occurring in the NISAT I divers was not reported to occur in the divers studied by Saltzman.

It is conceivable that the symptoms represented a variant of the high pressure nervous syndrome. Although the high pressure nervous syndrome is characterized by tremor, sommolence, ECG changes, and rapid compression rates to depths beyond 7.00 ATA (198 fswg), nausea, dizziness, and occasional vertigo have been reported to occur (10). Since the symptoms began very shortly after the subjects started to breathe the normoxic gas mixture at 7.00 ATA (198 fswg), hypoxia of central nervous system tissue could be considered a possible causative factor. The literature supports the hypoxia theory first by documenting the existence of a decrement in human performance under hypoxic conditions (22). Second, medium sized animals experience behavioral changes of paralysis when subjected to normoxic gas mixtures (P_{IO_2} = 0.21 ATA) at depths greater than 10.09 ATA (300 fswg) in hyperbaric chambers (4). When the P_{IO_2} is raised at depth, the paralytic behavior of these animals is reversed and they resume normal activity. Third, recent studies in mice showed a decrement in spontaneous running activity under well controlled environmental conditions at depths of 100 ATA (3,300 fswg) while breathing normoxic gas mixtures (23). Based on these seemingly relevant literature citations, and the NISAT I diver's improved condition following the addition of oxygen to their breathing gas, it would seem reasonable to infer that low tissue oxygen levels caused the symptoms. This notion is supported by electrocardiographic findings obtained under resting conditions (31). It is interesting that the nausea did not recur during exercise in the NISAT I divers. Perhaps the earlier discomfort was not caused by tissue hypoxia, but rather by the sudden lowering of PI_{O_2} combined with other physiological stressors. Such stressors might include the rate of compression, the respiration of dense gas, the tissue uptake of inert gas (3, 6), or fluid compartment shifts in response to inert gas induced osmosis (9). The fact that NISAT I subjects continued to suffer from nausea until dive day 3 would support the contention that intensified human autonomic reflexes adapted to the unusual environment over several days' time. If this "combined stressor" concept was operative, perhaps modification of the compression rate and/or inspired oxygen concentration would have alleviated the distressful symptoms and allowed for the accomplishment of meaningful work when the divers reached saturation depth. Although the literature provides information allowing one to differentiate the possible cause of the early unpleasant symptoms in NISAT I, the objective information available is not strong enough to conclude the most likely mechanism.

The results of the NISAT I study at 7.00 ATA (198 fswg) indicate that at this level of pressure ventilatory limitations appear also under resting conditions as shown in the increased alveolar CO_2 tensions. It was at 7.00 ATA (198 fswg) that exercise tests had to be terminated prematurely for medical reasons because of appearance of arrhythmias in the electrocardiogram. The increase in the heights of the P and T waves and shortening of the Q-T interval represent the normal pattern of electrocardiographic changes during exercise (28). The slight S-T segment change observed during maximal work loads is also a common feature in normal subjects (28, 30). The pathologic flat or square wave S-T depression typical of ischemia (15) was not observed in any of the subjects.

The significance of exercise-induced cardiac arrhythmias during saturation diving in this setting, as in the clinical situation with normal individuals, is uncertain. The PAC's occasionally seen during exercise in SHAD III and NISAT I are common in both emotional and physical stress (1, 16). The significance of the PVC's observed in diver T during exercise in NISAT I remains unclear. This individual was quite active physically, working as a diving instructor and commercial diver in his spare time; he had no history of cardiovascular symptomatology. Numerous stress tests before and after the dive failed to reveal any PVC's. There is little doubt that the man was stressed by the work load at this gas density and the possibility that these exercise-induced PVC's indicate previously unrecognized coronary insufficiency brought on by the added stress of the dive needs consideration. However, the typical S-T segment changes associated with myocardial ischemia were not observed.

PVC's are observed in normal individuals during exercise (1, 11, 12, and 19). The mechanism of such arrhythmias remains unclear. It is the opinion of some investigators (2, 26) that exercise-induced PVC's represent an abnormal finding, whereas others (17, 18, and 29) have denied clinical significance to this occurrence. Kosowsky, et al (11) feel that the mere occurrence of ventricular ectopic activity during exercise does not necessarily identify a group highly susceptible to fatal arrhythmias. The occurrence of this type of ectopic activity in the hyperbaric environment is certainly of significance, particularly since it occurs simultaneously with ventilatory constraints and CO_2 retention. Figures 4 and 5 exhibit a unique set of ECG records with PVC's obtained on the same subject during and after exercise tests of 125 watts at 7.00 ATA (198 fswg) on two subsequent dive days.

Figure 4 shows PVC's appearing in the recovery phase following the termination of the exercise tests by the subject due to physical exhaustion. Under these circumstances, one has to assume that in this subject PVC's are related to physical exhaustion. Figure 5 shows PVC's during and after a 125-watt exercise test, which was stopped by the physician because of the association of signs of exhaustion (cold sweat) and the appearance of PVC's.

It has been previously reported that electrocardiographic changes occurred under resting conditions during the two deepest dives to 4.03 ATA (100 fswg) and 7.00 (198 fswg). They were considered to represent right-ventricular conduction delay compatiable with right-ventricular strain. Dr. Ian Caldor (personal communication) observed autopsy evidence of mild ventricular hypertrophy and pulmonary vasculature changes consistent with pulmonary hypertension in a 24-year-old British professional diver dying of unrelated causes (31).

Under conditions of increased respiratory work due to increased gas density, a significant load is put on the respiratory system, the pulmonary circulation and the right heart. The simultaneous study of respiratory functions and electrocardiographic changes in exercise during these dive series (SHAD I, II, III, and NISAT I) show that constraints on pulmonary and circulatory functions are correlated with each other. Arrhythmias were only found in those exercise tests in which the ventilatory response was decreased and CO_2 retention observed.

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Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER
NSMRL Report 956

2. GOVT ACCESSION NO.

3. RECIPIENT'S CATALOG NUMBER

4. TITLE (and Subtitle)
CO_2 RETENTION AND ECG CHANGES IN EXERCISE DURING PROLONGED HYPERBARIC N_2-O_2 BREATHING

5. TYPE OF REPORT & PERIOD COVERED
Interim report

6. PERFORMING ORG. REPORT NUMBER
NSMRL Report 956

7. AUTHOR(s)
Karl E. Schaefer, James H. Dougherty, Jr., James M. Wilson, Russel L. Frayre and Douglas R. Knight

8. CONTRACT OR GRANT NUMBER(s)

9. PERFORMING ORGANIZATION NAME AND ADDRESS
Naval Submarine Medical Research Laboratory
Box 900 Naval Submarine Base New London
Groton, CT 06349

10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
M0099-PN.002-7060

11. CONTROLLING OFFICE NAME AND ADDRESS
Naval Submarine Medical Research Laboratory
Box 900 Naval Submarine Base New London
Groton, CT 06349

12. REPORT DATE
30 November 1982

13. NUMBER OF PAGES
21

14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)
Naval Medical Research and Development Command
National Naval Medical Center
Bethesda, MD 20814

15. SECURITY CLASS. (of this report)
Unclassified

15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distirbution unlimited

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)
CO_2 retention; ECG changes; N_2-O_2 breathing;

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Respiratory function (V_E, $\dot{V}O_2$, $\dot{V}CO_2$, R, and P_{ACO_2}) was measured in ten subjects at rest and exercise during prolonged hyperbaric chamber exposure to 2.52, 2.82, 4.03, and 7.00 atmospheres absolute (ATA). At 4.03 ATA the ventilatory response to exercise was found depressed at 150 watts. Increased P_{ACO_2} indicated CO_2 retention. At 7.00 ATA there was a slight but significant

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elevation of $P_{A}CO_2$ at rest and a depression of the ventilatory response to exercise at both 50 and 125 watts associated with a marked CO_2 retention.

Arrythmias were found at 4.03 and 7.00 ATA with workloads of 150 and 125 watts, respectively. At 4.03 ATA, premature atrial contractions (PAC) were noted at 150 watts in two subjects during four separate testing sessions. At 7.00 ATA, PAC's were observed at 125 watts in two subjects. One subject developed premature ventricular contractions (PVS's) during three different tests at 125 watts. Arrythmias occurred only in those exercise tests which produced a marked CO_2 retention at increased pressure.